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ELI LILLY AND COMPANY

By _____
Signature

October 17, 1986
Date

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	David B. Anderson, et al.	
Serial No.:	811,059	
Filed :	December 19, 1985	Group Art Unit: 125
For :	GROWTH PROMOTION	Examiner: F. Waddell
Docket No.:	X-5683B	

DECLARATION UNDER 37 C.F.R. 1.132

Commissioner of Patents and Trademarks

Washington, D.C. 20231

Sir:

I, Dr. D. Jay Jones, hereby declare and say as follows:

I attended Purdue University in Lafayette, Indiana, from which I received a Bachelor of Science degree in Agricultural Economics in 1967, Master of Science degree in Animal Science in 1969, and a Doctor of Philosphy degree in Animal Science in 1972.

I joined Eli Lilly and Company in 1976 as a Technical Specialist. I was named an Animal Science Representative in 1981, and became Research Scientist in 1983. Since 1981, I have conducted and supervised basic research in the area of animal nutrition.

I have had 30 years of experience working with animal nutrition of swine, and am thoroughly familiar with the literature concerning growth performance in animals such as swine. I am familiar with carcass quality, such as the amount of leanness in an animal, and the methods available in the art to improve the percent of fat free muscle.

I am familiar with the subject matter claimed in the above-captioned patent application, and I have worked extensively with one compound embraced within that application, namely compound 31537. I am also familiar with a compound described by Mills et al. in U.S. Patent No. 4,391,826, namely compound 79771, which is described by Mills et al. as being an antiobesity agent and effective for improving leanness in domesticated animals.

I conducted and supervised the following test to compare the biological effects of 31537 to those of 79771 compared to untreated control animals. We selected a group of cross-bred pigs of the type routinely employed for commercial pork production. We divided the pigs into three groups of 35 each. All animals received food and water ad libitum. One group of 35 animals received an oral dosing of 10 ppm of invention compound 31537, and another group of 35 animals received a dosing of 10 ppm of Mills et al. 79771. The third group of animals served as controls and did not receive any medication. Each of the groups had an average animal weight of 146 pounds at the beginning of the test, and each animal was maintained in the test until it reached about 231 pounds at which time it was slaughtered and analyzed. Both the control animals and those receiving 79771 required an average length of treatment of 57 days in order to reach the 231 pound finish weight. The animals receiving 31537 reached the desired weight in only 51 days. The average daily gain (ADG) of each treatment group was determined by subtracting the average final weight for the group from the average initial weight, and dividing it by the number of days of treatment which that particular group had received. The results of the growth phase of the study are presented in Table I.

Table 1

Treatment	No. Pigs[1]	Ave. Init. Wt. (lbs)	Ave. Final Wt. (lbs)	ADG (lbs)	ADF (lbs)	Feed/Gain
Control	35	146	231.5	1.50	5.47	3.64
79771, 10 ppm	35	146	230.5	1.48 (-1.3%)	5.49 (+.3%)	3.72 (+2.2%)
31537, 10 ppm	35	146	231.3	1.68 (+12%)	5.30 (-3.1%)	3.16 (-13.2%)

[1] Three pigs were removed from this trial (one from each treatment group) due to chronic slow growth.

Figures in parentheses are percent change from control.

Table I shows that the group receiving the invention compound 31537 had an average daily gain of 1.68 lbs., 12% more gain than the untreated controls. The group receiving the Mills et al. compound 79771 actually had a reduction in average daily gain of 1.3% compared to untreated controls.

The term referred to as average daily feed (ADF) is the total amount of feed consumed by the animals divided by the number of days they were on treatment. The table establishes that the animals receiving invention compound 31537 actually had a reduction in average daily feed intake of 3.1% compared to untreated controls, whereas the group receiving the Mills et al. compound 79771 were about the same as untreated controls, showing an increase in average daily feed of 0.3%.

Perhaps the most important number that reflects the utility of the invention compound is what is referred to as the feed-to-gain ratio (F/G), which is the effect on feed efficiency exhibited by a particular compound. The lower the feed-to-gain ratio, the more efficient the animal is in converting consumed food to meat. The group receiving the invention compound 31537

had a feed efficiency improvement of 13.2% relative to untreated controls, whereas the group receiving the Mills et al. compound 79771 actually showed a reduction in efficiency of 2.2%.

Table 2 below shows the carcass characteristics of the three test groups. The data reported in the table were collected at the time of slaughter of the animals. The animals were analyzed according to the methods described by Fahey et al. in J. Animal Science, Vol. 44, No. 1, 1977 (pp 8-17); and pp 3-18 of "Procedures to Evaluate Market Hog Performance", 2nd Edition, 1983, National Pork Producers Council. A copy of each reference is attached as part of this Declaration. All of the animals in each of the three groups were slaughtered at about 231 pounds, this being the normal finish weight for animals in the commercial pork production business in the U.S.

Table 2

Treatment	Pigs	Live Slaughter Wt. (lbs)	Dressing Percent	Leaf Fat (lbs)	10th Rib Fat Depth (in)	10th Rib Loin-Eye (sq. in.)	Est. % Fat Free Muscle[1]
Control	35	231.5	73.5	3.00	1.22	5.19	48.7
79771, 10 ppm	35	230.3	73.2 (-0.4%)	3.04 (+1.3%)	1.17 (-4.1%)	5.28 (+1.7%)	49.4 (+1.4%)
31537, 10 ppm	35	231.3	74.0 (+0.7%)	2.62 (-12.7%)	1.04 (-14.8%)	6.04 (+16.4%)	52.5 (+7.8%)

[1] Est. percent fat free muscle = 44.4 + (2.73 x 10th rib loin-eye area) - (8.06 x 10th rib fat depth).

Figures in parentheses are percent change from control.

Dressing percent is the carcass weight divided by live animal weight x 100. Table 2 shows that the group receiving the invention compound 31537 had an improved dressing percent,

whereas the group receiving the Mills et al. compound 79771 had a slight reduction in dressing percent.

The indication of leanness comes from a measurement of the fat that is referred to as leaf fat and the tenth rib fat depth. The leaf fat is simply the fat on the inside wall of the body in the kidney area and generally is considered waste, and is routinely used in the pork industry as an indication of wastage. Table 2 establishes that the group of animals receiving the invention compound 31537 had a reduction of 12.7% in the amount of leaf fat relative to untreated controls. The group receiving the Mills et al. compound 79771 actually had a greater amount of leaf fat, namely 1.3%, relative to untreated controls.

The fat depth measured at the tenth rib is a further indication of the leanness of an animal. As fat depth decreases, leanness increases. The results given in Table 2 are an average of measurements taken on both sides of the carcass when it was split down the center following slaughter. The data establish that animals receiving the invention compound 31537 had a reduction in the tenth rib fat depth of 14.8% relative to controls, whereas those animals receiving the Mills et al. compound 79771 exhibited only a 4.1% reduction in tenth rib fat depth.

Another measurement of leanness is loin-eye area measured between the tenth and eleventh rib. An increase in the amount of loin-eye area is synonymous to an increase in leanness. The data in Table 2 establishes that animals receiving the invention compound 31537 exhibited an average of 16.4% increase in loin-eye area, whereas those animals receiving the Mills et al. compound 79771 exhibited only a 1.7% increase in the loin-eye area.

The overall estimated percent of fat free muscle in an animal is arrived at by a standard formula that is used in the

industry (see Fahey et al., supra) and is an indication of the amount of leanness in useable meat. The estimated percent of fat free muscle is really the key indicator of carcass leanness. The data in Table 2 establish that the group of animals receiving the invention compound 31537 exhibited a 7.8% increase in the percent of fat free muscle. Animals receiving the Mills et al. 79771 exhibited a 1.4% increase in fat free muscle relative to controls.

The results of the studies I have conducted with 31537 and 79771 demonstrate to me that 31537 causes an unexpectedly greater benefit on animals than does 79771. The benefits are in terms of improved average daily gain, improved feed efficiency, and improved carcass leanness.

I further declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both (18 U.S.C.1001), and may jeopardize the validity of the application or any patent issuing thereon.

October 17, 1986
Date

D. Jay Jones